

Melkersson-Rosenthal syndrome: Still arousing clinician interest!

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Abstract

Melkersson-Rosenthal syndrome (MRS) is a rare neuromucocutaneous syndrome. It is a rare orofacial granulomatosis of controversial etiology, marked by the triad of recurrent nonpitting orofacial edema, recurrent facial palsy and plicated tongue. Through two clinical cases, we present in this article the clinical features and the diagnostic approach that clinicians should follow when faced with this pathology.

Keywords: Diagnosis; etiopathogenesis; Melkersson-Rosenthal syndrome; treatment

INTRODUCTION

Melkersson-Rosenthal syndrome (MRS) is a rare neuro-mucocutaneous syndrome of an unidentified etiopathogenesis. It is a rare facial granulomatosis classically defined by the triad of labial edema, peripheral facial palsy (FP) and plicated or scrotal tongue. The diagnosis is based on a set of clinical and histological arguments which reveals lymphoepitheloid or sometimes non-caseating giganto-cellular granulomas. The treatment is not well codified, because MRS is a complex entity which is difficult to treat due to its clinical polymorphism and the lack of identified etiopathogenesis. In the light of two clinical cases of MRS, this article aims to discuss, based on data from the literature, the different diagnostic and therapeutic possibilities in case of clinical manifestations considered to be characteristic of MRS.

CASE REPORT

Case 1

A 52-year-old female patient with a medical history of resolving peripheral facial palsy was admitted for recurrent rocking facial paralysis. Neurological examination found a hemi spasm, bilateral facial blepharo spasm predominantly on the right associated with episodes of migraine headaches and nonpitting face edema. In addition to, the importance of the facial hemi-spasm on the right, we noted the existence of a plicated tongue (Figure 1) and facial edema. We immediately retained the diagnosis of MRS. The treatment included two months

of oral corticosteroids (prednisone 1mg/kg/day with rapid decrease), motor rehabilitation and botulinum toxin injections which improved facial asymmetry and resolved labial edema.



Figure 1. Plicated (or scrotal) tongue

Case 2

A 31-year-old woman was admitted for sudden onset right facial palsy, progressing for 3 days without associated auditory or vestibular signs. Physical examination revealed right peripheral facial palsy (Figure 2), edema of the lips and a plicated tongue. Biological assessment was without abnormalities. Tonal audiometry was normal.

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Pathological examination of accessory salivary glands biopsy was without abnormality. The diagnosis of MRS was retained. The treatment was based on oral corticosteroid therapy and motor rehabilitation. The evolution was marked by an improvement of the facial palsy and disappearance of labial edema.



Figure 2. Right peripheral facial palsy

DISCUSSION

The history of RMS dates back to 1928, when Melkersson described facial edema and facial paralysis in a young female patient and suggested that there is a relationship between the two symptoms. In 1931, Rosenthal added the plicated tongue. The triad will be designated, in 1949, under the name of MRS. It occurs in young adults, most often after the end of the second decade, without a predominance of sex or race (1).

MRS pathogenesis remains unknown. Several hypotheses have been evoked: the inflammatory hypothesis suggesting the presence of circulating non-specific antigens which could cause vasomotor disorders of the small vessels of the cephalic end, giving subcutaneous and nerve sheaths edema, the lymphatic drainage abnormalities, allergic phenomena, bacterial or viral origin (herpes, toxoplasmosis, syphilis, etc.) (2,3).

The complete triad of MRS is less common than Miescher's cheilitis which is considered a monosymptomatic form of MRS or oligosymptomatic forms (4). MRS is characterized by its clinical polymorphism in which orofacial edema emerges, which is the major sign of the syndrome and sufficient to suggest the diagnosis (5). Plicated tongue is no longer considered a cardinal sign of the disease but as an evocative sign when combined with other cardinal signs. There is also chronological variability as two symptoms can appear simultaneously or many years apart (5). A deep biopsy of the lip with histological study of the edematous tissue is of great help in guiding the diagnosis. It expects to visualize the relationship between granulomas and venous or lymphatic vessels which signify the obliterating epithelioid endolymphangitis which is pathognomonic of MRS. However; results are inconsistent and may vary within the same patient. Normality of the examination does not rule out the diagnosis (6,7).

In 1990, Meisel-Stosiek and Hornstein proposed a classification which accounts for the very polymorphic

clinical manifestations of this syndrome (Table 1). A typical MRS has symptoms of the 1st, 2nd and 3rd order (1,6).

Table 1. Major and minor manifestations of the MRS (1,6)

1 st order signs	2 nd order signs	3 rd order signs	Diagnosis
Facial palsy + labial or facial edema of characteristic histological appearance	With or without plicated tongue		Complete MRS
Edematous lesions with a characteristic histological appearance			incomplete but a sure MRS
Facial palsy	Edema of uncharacteristic histological appearance		incomplete but a sure MRS
	Edema of uncharacteristic histological appearance + plicated tongue		Incomplete but probable MRS
	Edema of uncharacteristic histological appearance + two 2 nd order signs		Incomplete but probable MRS
	Edema of uncharacteristic histological appearance + one 2 nd order sign		Incomplete and doubtful MRS
	Uncharacteristic histologic lesions	three signs of 3 rd order	Incomplete and doubtful MRS
	Uncharacteristic histologic lesions		unlikely MRS

1st order signs: facial palsy, edema of characteristic histological appearance.

2nd order signs: plicated tongue, edema of uncharacteristic histological appearance, migraine-like headache, involvement of other cranial nerves.

3rd order signs: buccofacial vegetative symptoms, psychiatric symptoms

Major or 1st order symptoms

- The buccofacial edema is sometimes initial and often asymmetric. It is at first intermittent, then permanent; it can be extraoral and involve the lips, cheeks, eyelids or else it is intraoral and affect the gum, the cheek mucosa, the tongue. Labial edema is present in 70% of cases of MRS; it mainly affects the upper lip and occurs rather abruptly. Gingival enlargement may be the first manifestation of granulomatosis (8,9).

- Peripheral facial palsy appears after one or more episodes of edema. Sometimes it can occur months or even years before the edema. It appears either suddenly or gradually in one to two days. It is generally unilateral and exceptionally bilateral (9,10). It involves all the muscles of the face. The side affected by paralysis classically corresponds to that affected by edema (10). It can be accompanied by other nerve damage resulting in painful hyperacusis, ageusia involving the anterior two-thirds of the tongue, inflexion of lacrimal, nasal and salivary secretions.

2nd and 3rd order symptoms

- The tongue is plicated or scrotal in 20 to 60% of cases (6). It can start around 4 years old, and sometimes could already be present at birth. It would be transmitted according to an irregular autosomal dominant mode and seems to correlate with a geographic tongue which, most often, precedes it in time. The plicated tongue is therefore a characteristic sign but without diagnostic significance (6).

- Neurovegetative signs: tearing or dry eyes, hypersialorrhea or asialia, dysgeusia, hyperacusis, sweating disorders. Migraines, paresthesias and mood disturbances have also been reported (8). Optic nerve damage and retinal vessel abnormalities have been observed.

- There may be two histological types: the granulomatous type characterized by the presence of epitheliogigantocellular granulomas without caseous necrosis, which resemble sarcoidotic granulomas (11). The lymphonodular plasmacytic type, which is seen especially in easily edematous tissues such as the eyelids (8).

The main differential diagnoses are sarcoidosis and Crohn's disease. However, other diseases can be added to the list of differential diagnoses such as tuberculosis, tuberculoid leprosy, pyostomatitis vegetans, contact hypersensitivity reactions, acquired and hereditary angioedema, and lupus vulgaris (12).

There is no basic treatment or specific treatment due to the existence of many pathophysiological theories (infectious, immuno-allergic and genetic). It is essentially symptomatic and depends on aesthetic repercussions and clinical signs. Oral corticosteroid therapy is the least disappointing at the time of edematous outbreaks and is compulsory in case of FP. Clofazimine, tetracyclines, metronidazole and dapsone are to be used as second line. A few case reports show the effectiveness of thalidomide

and anti-TNF α . Reduction cheiloplasty is indicated only in cases of edema that has not developed for at least six months (7). In case of FP, systemic or intralesional corticosteroid therapy is the treatment of choice (13). Botulinum toxin has revolutionized the results obtained by improving facial symmetry. The toxin can be used either on the healthy side of the face to treat compensatory hyperactivity on the non-paralyzed side of the face, or on the paralyzed side (in spastic forms) to treat co-contractions and spasms on the affected side of the face (14). This treatment will of course have to be supplemented by functional rehabilitation. Neurolysis or surgical nerve decompression may be discussed in the absence of good outcome (15).

CONCLUSION

MRS is a rare disease that continues to represent a diagnostic and therapeutic challenge for clinicians. There are many therapeutic proposals, but they only partially meet the expectations of patients. A better understanding of the physiopathological mechanisms would make it possible to improve the management of these patients who often present a significant aesthetic damage.

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